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Poisoning severity score, APACHE II and GCS: Effective clinical indices for estimating severity and predicting outcome of acute organophosphorus and carbamate poisoning

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ABSTRACT

Self-poisoning with organophosphorus (OP) compounds is a major cause of morbidity and mortality across South Asian countries. To develop uniform and effective management guidelines, the severity of acute OP poisoning should be assessed through scientific methods and a clinical database should be maintained. A prospective descriptive survey was carried out to assess the utility of severity scales in predicting the outcome of 71 organophosphate (OP) and carbamate poisoning patients admitted during a one year period at the Kasturba Hospital, Manipal, India. The Glasgow coma scale (GCS) scores, acute physiology and chronic health evaluation II (APACHE II) scores, predicted mortality rate (PMR) and Poisoning severity score (PSS) were estimated within 24 h of admission. Significant correlation ($P < 0.05$) between PSS and GCS and APACHE II and PMR scores were observed with the PSS scores predicting mortality significantly ($P \leqslant 0.001$). A total of 84.5% patients improved after treatment while 8.5% of the patients were discharged with severe morbidity. The mortality rate was 7.0%. Suicidal poisoning was observed to be the major cause (80.2%), while other reasons attributed were occupational (9.1%), accidental (6.6%), homicidal (1.6%) and unknown (2.5%) reasons. This study highlights the application of clinical indices like GCS, APACHE, PMR and severity scores in predicting mortality and may be considered for planning standard treatment guidelines.

1. Introduction

Acute organophosphate (OP) poisoning, due to intentional self harm exerts a major burden on the health care system and is responsible for great morbidity and mortality in developing countries. Because of their easy availability, organophosphorus (OP) compounds and other pesticides are commonly used for suicide.[1] Intentional ingestion of OP pesticides has been common for the past 40 years and is now the most preferred form of poisoning among poorer people across the central and southern parts of India.[2] Gunnell et al.[3] conservatively estimates that there are 258,234 (plausible range 233,997–325,907) deaths from pesticide self-poisoning worldwide each year, accounting for 30% (range 27–37%) of suicides globally. Official data from India probably underestimate the incidence of suicides; applying evidence-based corrections to India's official data, the estimate for world suicides using pesticides increases to 371,594 (range 347,357–439,267).[3] Though OP compounds are the cause for most self-poisoning deaths in southern and central India, there fails to be any systematic reporting of these cases.[4] The adult mortality rate due to deliberate self harm in rural South India is 0.97 per 1000 persons per year and almost equals to that attributed to infectious diseases. Only 70 to 80% of patients admitted to hospitals due to OP poisoning survive.[5]

There is a greater need for understanding the clinical characteristics of OP and carbamate poisoning, since in the majority of situations, the exact causative agents remain unknown and there is a lack of analytical assistance in most of the primary health care systems. Majority of the physicians depend purely on clinical signs and symptoms as a guide for diagnosis. However, the onset of symptoms may take some time to develop, by then the toxicity might become irreversible or even fatal. Intentional OP poisoning is a medical emergency which requires prompt treatment.[6] Since the ingestion of OP pesticides is responsible for the deaths of

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thousands of people in rural Asia every year, it is essential to establish an effective management strategy for such cases of poisoning.

A number of systems have been proposed for predicting outcome in OP poisoning. The International Program on Chemical Safety (IPCS)/EC/EAPCCT Poison Severity Score (IPCS PSS) was developed by the International Program on Chemical Safety, the European Community, and the European Association of Poisons Centers and Clinical Toxicologists to create a scoring system that produces a qualitative evaluation of the morbidity caused by different forms of poisoning.[7] The utility of the Glasgow coma scale (GCS), the acute physiology and chronic health evaluation (APACHE II) and the Poisoning Severity Score (PSS) in estimating severity and clinical prognosis of OP poisoning has seldom been applied to patients of the Indian subcontinent. Studies are warranted to assess the clinical characteristics, severity, treatment and outcome so as to assist decision makers in choosing the type and extent of therapy required and to find ways to bring down the number of deaths due to self harm. There is a need to assess the usefulness of the GCS, APACHE II, Predicted Mortality Rate and the International Program on Chemical Safety Poison Severity Score (IPCS PSS) to predict death in patients poisoned by OP pesticides.[8] Such survey programs which help in identifying and reporting the exposures and associated health hazards assist in the design of effective preventive and management strategies. Identification of high death risk in patients soon after presentation, allows more intensive monitoring and treatment. A simple system based on clinical features is likely to be most useful in low income countries where the majority of OP poisoning occurs.[9] Hence, a 1 year prospective study was undertaken to assess the correlation of severity scores with clinical symptoms, prognosis and outcome of OP poisoning cases following admission to a tertiary care hospital of South India.

2. Materials and methods

A prospective observational study was conducted in the emergency department of Kasturba Hospital, Manipal, Karnataka, India, for a period of one year between January and December 2005. The severity of all acute, OP and carbamate poisoning cases were evaluated irrespective of age and sex. Poisoning due to other pesticides, herbicides, drugs, chemicals, etc. were excluded. Epidemiological characteristics and risk data were collected from medical files and documented in the case record forms. The data including demographic information (age, sex), toxic substances involved, type of poisoning, clinical symptoms, laboratory tests and patient outcome were evaluated. The state of consciousness and mental status (extent of mental injury) at the time of admission were assessed using the Glasgow coma scale (GCS).[10] The Glasgow coma score (Table 1) was assigned, based on three responses, i.e. best eye response, best verbal response, and best motor response. A maximum of 15 and a minimum of three were assigned. The lowest possible GCS score (the sum) was three (deep coma or death), while the highest score was 15 (fully awake person).

The prognosis and predicted mortality rate was estimated using acute physiological and chronic health evaluation scale (APACHE II scale) (Table 2).[11,12] The APACHE II score was calculated from 12 routine physiological and laboratory measurements made during the first 24 h (Table 2). The score for each parameter was assigned from 0 to 4, with 0 being normal and four being the most abnormal. The sum of these values were added to a mark adjusting for patient age and a mark adjusting for chronic health problems (severe organ insufficiency or immuno-compromised patients), to arrive at the APACHE II score. The resulting point score was interpreted in relation to the illness of the patient. The measurement was made during the first 24 h following admission to the emergency ward and resulted in an integer point score between 0 and 71. The predicted mortality rate was calculated based on the APACHE II score.

The severity of poisoning was assessed using the IPCS-poisoning severity scale (IPCS PSS) (Table 3) recommended by the WHO-International Program on Chemical Safety (IPCS)/EC/EAPCCT) and adopted from Persson et al. (1998).[13] Occurrence of a particular symptom was checked against the chart and graded. The severity grading assigned to a case was determined by the most severe symptom(s) or signs(s) observed. The severity was graded from 0 to 4, ranging from no toxicity to severe life threatening symptoms and death and taking into consideration clinical signs/symptoms and/or laboratory data. The factors affecting PSS scores, *viz.* prehospitalization period, demographical variables, type of poison ingested, average butyrylcholinesterase, and manner of exposure were evaluated. The GCS, APACHE II score and IPCS PSS were estimated within 24 h from the day of admission and represents the worst score, observed on the day of admission.

Table 1
The Glasgow coma scale provides a score in the range 3–15; patients with scores of 3–8 are usually said to be in a coma. The total score is the sum of the scores in three categories.

Aduult score			
Eye opening response		Spontaneous–open with blinking at baseline	Four points
		Opens to verbal command, speech, or shout	Three points
		Opens to pain, not applied to face	Two points
		None	One point
Verbal response		Oriented	Five points
		Confused conversation, but able to answer questions	Four points
		Inappropriate responses, words discernible	Three points
		Incomprehensible speech	Two points
		None	One point
Motor response		Obeys commands for movement	Six points
		Purposeful movement to painful stimulus	Five points
		Withdraws from pain	Four points
		Abnormal (spastic) flexion, decorticate posture	Three points
		Extensor (rigid) response, decerebrate posture	Two points
		None	One point
Score	2–5 Years	0–23 Mos.	
For children under five, the verbal response criteria are adjusted as follow			
5	Appropriate words or phrases	Smiles or coos appropriately	
4	Inappropriate words	Cries and consolable	
3	Persistent cries and/or screams	Persistent inappropriate crying and/or screaming	
2	Grunts	Grunts or is agitated or restless	
1	No response	No response	

Table 2
APACHE II scoring system.[a]

	Physiologic variable[b]	Point score								
		+4	+3	+2	+1	0	+1	+2	+3	+4
1	Temperature	⩾41°	39–40.9°	–	38.5–38.9°	36–38.4°	34–35.9°	32–33.9°	30–31.9°	⩽29.9°
2	Mean arterial pressure (mm Hg)	⩾160	130–159	110–129	–	70–109	–	50–69	–	⩽49
3	Heart rate	⩾180	14O–179	110–139	–	70-109	–	55–69	40–54	⩽39
4	Respiratory rate(non-ventilated or ventilated)	⩾50	35–49	–	25–34	12–24	10–11	6-9	–	⩽5
5	Oxygenation:									
	a) $FiO_2 \geqslant 0.5$: use A-aDO_2	⩾500	350–499	200–349	–	<200	–	–	–	–
	b) $FiO_2 < 0.5$: use PaO_2 (mm Hg)	–	–	–	–	>70	61–70	–	55–60	<55
6	Arterial pH	⩾7.7	7.6–7.69	–	7.5–7.59	7.33–7.49	–	7.25–7.32	7.15–7.24	<7.15
7	Serum Na (mMol/L)	⩾180	160–179	155–159	150–154	130–149	–	120–129	111–119	⩽110
8	Serum K (mMol/L)	⩾7	6–6.9	–	5.5–5.9	3.5-5.4	3–3.4	2.5–2.9	–	<2.5
9	Serum creatinine (mg/dL): double point score for acute renal failure	⩾++++3.5	2–3.4	1.5–1.9	–	0.6–1.4	–	<0.6	–	––
10	Hct (%)	⩾60	–	50–59.9	46–49.9	30–45.9	–	20–29.9	–	<20
11	WBC (in l000s)	⩾40	–	20–39.9	15–19.9	3–14.9	–	1–2.9	–	<1
12	Glasgow coma score (GCS)	Score = 15 minus actual GCS								
Acute physiology score is the sum of the 12 individual variable points										
Add 0 points for the age <44.2 points. 45–54 years: three points. 55–64 years: five points. 65–74 years: six points⩾75 years										
APACHE II score = acute physiology score + age points + chronic health points. Minimum score = 0; maximum score = 71. Increasing score is associated with increasinf = g risk of hospital death										
Add chronic health ststus points: two points if elective postoperative patient with immunocompromise or history of severe organ insufficiency: five points for nonoperative patient or emergency postperative patient with immunocompromise or severe organ insufficiency[c]										
13[d]	Serum HCO_3(venous-mMol/L) use only if no ABGs52	⩾52	41–51.9	–	32–40.9	22–31.9	–	18–21.9	15–17.9	<15

Adapted from Knaus WA. Draper EA. Wagner DP. Zimmermam JB: APACHE II: A severity of disease classification system. *Critial care medicine* 13: 818–829. 1985.
Interpretation of APACHE II scores (predicted mortality rate).
0–4 = ∼4% death rate 10–14 = ∼15% death rate 20–24 = ∼40% death rate 30–34 = ∼75% death rate.
5–9 = ∼8% death rate 15–19 = ∼25% death rate 25–29 = ∼55% death rate Over 34 = ∼85% death rate.

[a] APACHE II Score = acute physiology score + age points + chronic health points. Minimum score = 0; maximum score = 71. Increasing score is associated with increasing risk of hospital death.

[b] Choose worst value in the past 24 h.

[c] Chronic health status: Organ sufficiency (e.g. hepatic, cardiovascular, renal, pulmonary) or immuno-compromised state must have preceded current admission.

[d] Optional variable: use only if no ABGs.

The incidence of intermediate syndrome was assessed among the patients. Intermediate syndrome is a clinical entity that develops after cholinergic crises, 24–96 h after poisoning. It was diagnosed when the patient developed signs of marked weakness of neck flexon with the inability to lift the head from the pillow. This proved to be a reliable test to assess whether a patient was likely to develop respiratory muscle weakness. Cranial nerve palsies and proximal muscle weakness were also observed. There was a relative sparing of the distal muscle groups.[14]

Clinical outcome measures, including the period of hospitalization and clinical condition at the time of discharge were determined. The clinical outcomes were sorted out using three variables, namely, improved status, morbid state, or fatal outcome. The variable 'improved status' was defined as the state of complete recovery with no associated permanent physical or physiological abnormality. 'Morbidity state' was defined as a state of either clinically unstable vital functions or a disturbed physical, functional and physiological state. 'Fatality' was defined as a clinical state of brain death as certified by the physician. Factors affecting clinical outcome, *viz.* demographical factors, pre-hospitalization period, butyrylcholinesterase levels, GCS, APACHE II score, predicted mortality rate (PMR) and PSS were assessed.

3. Statistical analysis

The results were expressed as mean ± SD. The categorical data collected were summarized using proportions by chi-square (χ^2) test. The mean scores of different groups were compared using Kruskal–Wallis test. Pearson correlation was used to study the correlation between various scores and mortality. A probability of $P \leqslant 0.05$ was considered statistically significant. SPSS version 11 statistical software was used for evaluation.

4. Results

4.1. Patient demographics and exposure characteristics

Among a total of 91 (43.13%) pesticide-poisoning cases, OP poisoning accounted for 71 (33.65%) admissions including 54 (76.0%) males and 17 (23.9%) females. Majority of the poisoning occurred among the age group of 21–30 years ($n = 22$), ranging between 2–65 years with an average age of 31.23 ± 11.11 years (mean ± SD). Acute exposures were either suicidal ($n = 62$); accidental ($n = 5$); occupational ($n = 3$) or homicidal ($n = 1$) by nature. Majority of the patients resorting to self harm were males (76.06%) than females (3.94%). As seen in Table 4, methyl parathion of WHO-Class Ia (extremely hazardous chemicals) was the most commonly implicated OP compound accounting for 29 (40.8%) admissions.

4.2. Clinical characteristics

The average time lapse between exposure to the time of admission at the emergency department (pre-hospitalization period) was 3.27 ± 1.71 hours (range 0.5–7 h) with a median of 3.00 hours [IQR = 2–3]. The median plasma butyrylcholinesterase level measured in 68 cases was 295 IU/L and ranged from 60 to 8020 IU/L. It was observed that 39 patients developed signs of intermediate syndrome, with paralysis of proximal limb muscles, neck flexors, motor cranial nerves, and respiratory muscles, 24–96 h after poisoning, following a well-defined cholinergic phase. At the time of admission, the GCS score of less than eight was observed in 23 (32.4%) patients. A total of 40 (56.3%) patients required intubation and ventilator assistance, of whom 15 patients had a GCS score of <8, while 11 had a GCS score of ⩽6. Among those with GCS score of <8, four patients died, four patients were discharged with severe

Table 3
Signs and symptoms by severity category (Modelled after Persson et al., 1998).

Organ system	Severity category and code			
	Fatal Grade 4 Death	High severerity Grade 3 Severe or life-threatening (Severe)	Moderate severity Grade 2 Pronounced or prolonged signs or symptoms (Moderate)	Low severity Grade 1 Mild, transient, and spontaneously resolving symptoms (Mild)
Cardiovascular system		• Bradycardia/heart rate <40 for adults,< 60 for infants and children • Tachycardia HR>180 for adults, >190 infants/children, >200 in neonates • Cardiac arrest	• Bradycardia/HR 40–50 in adults, 60–80 in infants / children, 80–90 in neonates • Tachycardia/HR = 140–180 in adults, 160–190 infants/ children, 160–200 in neonates • Chest pain + hyperventilation, tachypnea • Conductance disturbance • Hypertension • Hypotension	
Respiratory system		• Cyanosis + Respiratory depression • Pulmonary edema • Respiratory arrest	• Abnormal pulmonary X-ray • Pleuritic chest pain/pain on deep breathing • Respiratory depression • Wheezing • Dyspnea, shortness of breath	• Cough • Upper respiratory pain, irritation • Dyspnea, shortness of breath
Nervous system		• Coma • Paralysis, generalized • Seizure	• Confusion • Hallucinations • Miosis with blurred vision • Seizure • Ataxia • Slurred speech • Syncope • Peripheral neuropathy	• Hyperactivity • Headache • Profuse sweating • Dizziness • Ataxia • Peripheral neuropathy
Gastrointestinal system		• Massive hemorrhage/perforation of gut	• Diarrhea • Malena • vomiting	• Abdominal pain, cramping • Anorexia • Constipation • Diarrhea • Nausea • Vomiting
Metabolism		• Acid Base disturbance (pH <7.15 or >7.7)	• Acid Base disturbance (pH = 7.15–7.24 or 7.60–7.69) • Elevated anion gap	• Fever
Renal system		• AnuriaRenal • Failure	• Hematuria • Oliguria • Proteinuria	Polyuria
Muscular system		• Muscle rigidity + elevated creatinine	• Fasciculations • Muscle rigidity • Muscle weakness	• Muscle weakness • Muscle pain
Local effects on skin		• Burns second degree (involving >50% of body surface area) • Burns, third degree (involving >20% of body surface area)	• Bullae • Burns, second degree (involving <50% of body surface area)Burns, third degree (involving <2% of body surface area)	• Skin edema/swelling, erythema, rash, irritation/pain, pruritis • Hives/urticaria
Local effects on eye		• Corneal ulcer/perforation	• Corneal abrasion • Ocular burn	• Lacrimation • Mydriasis • Miosis • Ocular pain/irritation/ Inflammation(diagnosis of conjunctivitis)
Other effects				• Fatigue • Malaise

Table 4
Trade and generic names and WHO classification of OP and carbamates pesticides implicated in poisoning.

S.No	Trade names	Chemical name	WHO Class	Frequency *N* (%)
	Organophosphates			
1.	Unknownsuspected OP poison	-NA-	–	14
2.	Metacid, Folidol	Methyl parathion	Ia	29 (40.8)
3.	Phoskil, Nuvacron, Monophos	Monocrotophos	Ib	4 (5.6)
4.	Ekalux	Quinalphos	II	4 (5.6)
5.	Rogur 30 E, Crogor	Dimethoate	II	4 (5.6)
6.	Lethal, piridane	chlorpyriphos	II	4 (5.6)
7.	Thimet, Phorate	Phorate	Ia	2 (2.8)
	Carbamates			
8.	Baygon, Hit	Propoxur	II	3 (4.2)
9.	Furadan, Carburan	Carbofuran	Ib	1 (1.4)
10.	Sevin	Carbaryl	II	1 (1.4)
	Unknown pesticide		–	5 (7.0)
	Total			71

Ia – Extremely hazardous; Ib – highly hazardous; II – moderately hazardous; III – slightly hazardous.

morbidity and 14 patients exhibited intermediate syndrome. The average GCS scores of intubated patients were significantly lower ($P < 0.05$) than those who were non-intubated. However, no significant association could be drawn between GCS and the need for ventilation support. The GCS scores were found to possess a significant ($P < 0.001$) negative linear relationship with APACHE II scores, PMR and PSS (Pearson correlation $r = -0.660$; $r = -0.636$; $r = -0.583$), respectively. Patients who had low GCS and higher APACHE and PMR scores correspondingly showed higher PSS severity scores. A significant ($p = 0.004$) negative correlation ($r = -0.339$) was observed between the GCS scores and the incidence of mortality.

The average APACHE II score was found to be 12.28 ± 5.29 and the average PMR was 16.76 ± 12.69%. A significant linear correlation was observed between the clinical outcome, the APACHE II scores (Pearson correlation $r = 0.347$) ($P = 0.003$) and the predicted mortality rate (Pearson correlation $r = 0.419$) ($p < 0.001$). APACHE II scores were found to exhibit a significant ($p < 0.001$) linear relationship with PSS scores ($r = 0.557$).

As seen in Table 5, majority $n = 37$ (52.1%) of the cases, had a PSS of grade 3, indicating severe and life threatening toxicity. Extremely severe toxicity leading to mortality (grade 4) was observed in 10 (14.08%) patients, among whom five died within the hospital while others died after discharge in a moribund state. Twenty cases (28.2%) showed grade 2 severity of moderate intensity; three patients (4.2%) had grade 1 severity of mild intensity. Majority of the males (53.1%) exhibited grade 3 severity while 16.7% males showed grade 4 (severe/lethality) severity. Among the females, grade 3 severity was observed in 47.06% and grade 4 severity in 5.8% of patients. The highest severity of poisoning was observed among the 21–30 year age group where 14 patients had grade 3 scores and three patients had grade 4 scores. Three deaths were reported in this group. In the 31–40 year age group, seven patients had grade 3 severity, three patients had grade 4 severity and two deaths were reported. Majority of the poisoning were due to intentional self harm with suicidal intentions. Patients due to occupational exposure ($n = 3$) exhibited, significantly ($p = 0.01$) higher median severity scores (PSS = 3) ($\chi^2 = 10.8$, df = 3) than those admitted due to either suicidal or accidental exposures. As observed in Table 6, 47 cases had a PSS grade of three or more. There was a significant ($p \leqslant 0.001$) correlation between mean GCS scores, APACHE II scores, and PMR with respect to mean PSS grades. However there was no significant association or linear correlation between plasma butyrylcholinesterase levels and PSS. PSS grades were significantly ($p < 0.05$) associated with the incidence of intermediate syndrome. Twenty five patients of grade 3 severity had intermediate syndrome, while all the 10 patients with grade 4 severity had intermediate syndrome. A statistically significant ($p < 0.001$) correlation was found between the PSS grades and the need for ventilation. Among the 40 patients ventilated, 28 patients had a severity score of three. While all the 10 patients with severity grade 4 needed ventilation, only one patient each with grades 1 and 2 severity needed ventilation. A significant linear correlation ($p = 0.024$) ($r = 0.269$) was observed between the time lapsed

Table 5
Effect of demography and manner of exposure on poisoning severity score.

Grade→	Poisoning severity score (PSS) (mean ± SD)	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Gender						
Male $N = 54$	2.8 ± 0.9	1 (1.9%)	3 (5.55%)	12 (22.2%)	29 (53.07%)	9 (16.67%)
Female $N = 17$	2.6 ± 0.6	–	–	8 (47.06%)	8 (47.06%)	1 (5.8%)
Age distribution						
0–10 years $N = 4$	2.5 ± 1.0	0	0	3	0	1
11–20 years $N = 11$	3.0 ± 0.7	0	2	4	5	0
21–30 years $N = 22$	2.8 ± 0.8	1	0	4	14	3
31–40 years $N = 16$	2.8 ± 0.7	0	0	6	7	3
41–50 years $N = 13$	2.7 ± 0.7	0	1	2	9	1
51–60 years $N = 3$	3.3 ± 0.6	0	0	0	2	1
61–70 years $N = 2$	3.0 ± 1.4	0	0	1	0	1
Manner of exposure						
Intentional self harm $N = 62$	2.7 ± 0.8	1	3	16	36	6
Accidental $N = 5$	2.8 ± 1.0	–	–	3	0	2
Occupational $N = 3$	3.6 ± 0.6 *	–	–		1	2
Homicidal $N = 1$	2.0	–	–	1	0	0
Total $N = 71$	2.7 ± 0.81	1	3	20	37	10

* $P < 0.05$ significantly different median PSS scores compared to other exposure groups (Kruskal–Wallis median test).

Table 6
Effect of clinical characteristics on poisoning severity score and its role in predicting outcome.

Grade→	Total	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Variables						
Pre-hospitalization period (mean ± SD)	3.3 ± 1.7	1.0 ± 0	2.8 ± 1.4	2.6 ± 1.6	3.6 ± 1.7	3.7 ± 1.9
Butyrylcholinesterase (mean ± SD)	3899.8 ± 4617.1	5535.0 ± 0	6596.0 ± 6435.8	5265.5 ± 6313.9	3143.1 ± 3272.5	2980.7 ± 4413.7
Glasgow coma score (mean ± SD)	10.3 ± 3.7*	15.0 ± 0	15.0 ± 0	12.8 ± 2.3	9.2 ± 3.4	7.3 ± 3.6
APACHE II score (mean ± SD)	12.3 ± 6.4*	3.0 ± 0	5.0 ± 4.4	7.6 ± 4.5	14.7 ± 5.4	15.9 ± 6.4
Predicted mortality rate (mean ± SD)	16.8 ± 12.7*	3.8 ± 0	5.7 ± 3.7	8.4 ± 5.8	20.6 ± 12.2	24.1 ± 15.6
Hospitalization period (mean ± SD)	13.6 ± 10.0*	3.0 ± 0	10.7 ± 2.1	10.9 ± 6.3	17.4 ± 11.5	6.6 ± 3.9
Improved (N)	60[a]	1	3	20	36	0
Morbidity (N)	6[a]	0	0	0	1	5
Mortality (N)	5[a]	0	0	0	0	5

The results are expressed as mean ± SD.
* $P < 0.001$ significant difference on comparison of median values between various poisoning severity groups (Kruskal–Wallis test).
[a] $P < 0.001$ significant association of values between various poisoning severity score groups (chi-square).

Table 7
Demographic factors affecting outcome.

Age range (years)	Male/female ratio	Mortality, $n = 5$	Morbidity, $n = 6$	Improved, $n = 60$
Gender				
Male	–	5	5	44
Female	–	0	1	16
Age groups				
0–10 years ($n = 4$)	2:2	1	0	3
11–20 years $n = 11$	6:5	2	0	9
21–30 $n = 22$	18:4	0	0	22
31–40 $n = 17$	12:5	0	1	16
41–50 $n = 12$	11:1	1	2	9
51–60 $n = 3$	3:0	0	2	1
61–70 $n = 2$	2:0	1	1	0
Total $n = 71$	53:17	5	6	60

n: Number of patients.

following exposure to admission (prehospitalization period) and the PSS. However there was no correlation observed between the pre-hospitalization period and the clinical outcome of the patients.

All the patients were treated with atropine infusion. Five cases were treated with continuous infusion of pralidoxime. Intravenous injection of glycopyrrolate which was employed as an antidote, concomitant to atropine infusions in 19 patients, significantly reduced the dose requirement of atropine, and also minimized the CNS toxicity of atropine. Gastric lavage with tap water was the most common decontamination procedure adopted and provided for all the patients irrespective of their time of admission, while activated charcoal was administered only to four patients.

4.3. Outcome assessment

Assessment of clinical outcome as described in Table 7 revealed that 60 patients (84.5%) recovered from illness while 6 (8.5%) were discharged without any improvement in a moribund state (with existing symptoms including respiratory failure, pneumonia, muscle paralysis and coma). Five patients succumbed to OP poisoning with a mortality rate of 7.04%. The mean age of dead cases was 25.6 ± 18.3 years. There were five readmissions for the management of associated complications following the poisoning treatment. The mean hospitalization period was 13.6 ± 6.9 days with a median of 11[8–18] [Interquartile range] days. No significant correlation was observed between PSS and the hospitalization period.

As seen in Table 8, there was a significant ($p < 0.001$) correlation between the PSS and mortality outcomes. However there was no significant difference of mean pre-hospitalization period, APACHE II scores, predicted mortality rate, butyrylcholinesterase levels between the outcome variables.

5. Discussion

The present study was designed to assess the effectiveness of various clinical scores including GCS, APACHE II and PSS to measure severity and predict the outcome of OP poisoning. The possible mortality risks at different exposure levels were predicted by evaluating the clinical effects, severity of mental injury, severity of physiological abnormality, poisoning severity and outcome. Severity scores were evaluated to assess the burden of illness following acute exposure. Acute OP poisoning is the most common reason for admission into the emergency department and medical intensive care unit (ICU). OP and carbamates constitute more than 80% of the overall poisoning cases admitted during the present study period. This finding corroborates with the results of many similar studies thereby showing that OPs and carbamates are the most common pesticides responsible for poisoning.[15]

Pesticides are currently classified by the WHO on the basis of their animal toxicity from Class Ia (extremely hazardous) through Class III (slightly hazardous), to compounds unlikely to cause ill health. The study revealed that extremely hazardous OPs belonging to Class I pesticides, including methyl parathion, monocrotophos, phorate, and carbamates together with carbofuran were implicated among most poisoning cases. Other compounds included quinolphos, dimethoate, chlorpyrifos and carbamates as well as propoxur and carbaryl belonging to Class II pesticides. Methyl parathion was the most commonly implicated OP among Class Ia pesticides and was responsible for four deaths. Similar findings were observed in a study carried out by Srinivas et al.[4] at Warangal, South India. Even without an increase in resources, significant opportunities exist for reducing mortality by better medical management and through stricter restrictions on the most toxic pesticides. Further studies are needed, to translate this knowledge into prevention.

Three patients with acute occupational exposure were admitted with an average severity grade of 3.7 ± 0.6. Potential for indirect and direct exposure exist among farmers and their next of kin who live in places where pesticides are used. The agricultural population of South India is exposed to the risk of pesticide residue, accidental exposure or impulsive acts of self harm. This is not only due to their easy accessibility, but also to their lack of knowledge with regard to storage, transportation and handling of pesticides.[16] A clinical database can help in identifying the health effects, severity, methods of treatment and outcome. This will be indispensable in the selection of effective methods to eliminate poisons from the system.

Even though a lowering of plasma butyrylcholinesterase was observed in the morbid group, this had no significant linear correlation with PSS scores. This observation contradicts other studies which show that the temporal profile of enzyme is significantly correlated to the clinical severity of poisoning.[17] Bobba et al.[18] had observed that sequential post exposure estimations of cholinesterase until 5 days did reveal some rise in the values, although

Table 8
Clinical factors affecting the outcome.

Groups	Plasma ChE (IU/L)	GCS	APACHE II score	Predicted mortality rate	Pre-hospitalization period (h)	Poisoning severity score (PSS)
Improved cases	4092.1 ± 4704.2	10.78 ± 3.6	11.52 ± 6.2	15.2 ± 11.6	14.8 ± 10.3	2.5 ± 0.7
Cases discharged with severe morbidity	524.0 ± 796.2	8.0 ± 3.5	17.3 ± 5.9	27.2 ± 14.2	7.8 ± 2.1	3.8 ± 0.4
Expired cases	5758.2 ± 4952.2	6.6 ± 3.6	15.4 ± 7.3	23.4 ± 18.3	5.4 ± 4,.9s	4.0 ± 0
Total	3900 ± 4617	10.2 ± 3.7	12.3 ± 5.29	16.8 ± 12.69	3.3 ± 1.71	2.7 ± 0.81
	$P = 0.65$	$P = 0.022^*$	$P = 0.058$	$P = 0.058$	$P = 0.217$	$P = 0.000^*$

The results are expressed as mean ± SD.
* $P < 0.001$ significant difference between various outcome variables (Kruskal–Wallis test).

there was substantial clinical improvement and concluded that the correlation of cholinesterase values with severity of symptoms are applicable only in the initial stages of acute poisoning.[18] Hence butyrylcholinesterase level determination can be used as a potential diagnostic tool, but cannot be counted reliable to predict the prognosis and mortality.

The duration of the pre-hospitalization period can influence the severity of poisoning at presentation. If the treatment is delayed, the initial peak blood level of poison may induce irreversible tissue damage to the organs. Early interventions are probably the most important determinants of survival in poisoning patients.[19] Our study revealed a moderate linear correlation ($r = 0.269$) between the pre-hospitalization period and severity scores. The proximity of health care workers with the abilities and facilities to treat pesticide poisoning is important, as is the availability of transport. As the primary health care centers in South India are not sufficiently equipped with first aid measures, there is a delay in obtaining immediate medical attention. The proximity of help available at the time of pesticide ingestion will often determine how quickly the person is brought to medical attention. The type of first aid actions administered may also affect the outcome.[20]

The Glasgow coma scale (GCS) is a neurological scale which appears to be a reliable objective way of recording the conscious state of a person, for initial as well as continuing assessment. The GCS score grades the patients with brain injury and helps in predicting their chances of neurological recovery. The GCS was first described in 1974 as a tool for monitoring the mental status of intensive care unit (ICU) patients with head injury. Over the past 30 years, the use of GCS has been expanded for monitoring of patients with altered mental status from causes other than head injury such as stroke and post cardiac arrest. Heard and Bebarta[21] demonstrated that GCS is a reliable tool for reporting the mental status of poisoning patients in the ED. One study reported the reliability of GCS for patients admitted due to poisoning in the ICU.[22] Clinicians now use GCS as the only neurological predictor in many prognostic systems, such as APACHE, APACHE II, APACHE III, acute physiology score (APS) and simplified acute physiology score (SAPS). For the assessment of severity and mortality of OP poisoning patients in an emergency situation, the GCS score is the best indicator (simple, less time consuming and effective). Several studies on therapies used in OP poisonings employed the GCS for evaluating brain injury.[23,24,10] In the present study, an inverse correlation ($r = -0.517$) observed between the GCS scores and PSS grades revealed its value in predicting severity. A significant ($P < 0.001$) negative linear correlation ($r = -0.5$) of GCS score with predicted mortality rate and also the observed clinical outcome was observed. Thus GCS can serve as a reliable tool for the evaluation of mental status, and the severity of poisoned patients in the emergency department. In this study no association was observed between the GCS scores and the need for ventilation. A GCS score of $\leqslant 8$ is generally accepted as an indication for intubation. In the present study, intubation and ventilatory support was considered only when the patient had respiratory failure (RF) and not on the basis of GCS values. Although a GCS score of less than or equal to eight has been shown to be a useful guideline for intubation of the poisoned patient, there is no accepted criterion/standard. Chan et al.[24] reported that, an initial GCS score of eight or less was found to be a useful guideline for intubation when used within a specific clinical context (sensitivity = 90%, specificity = 95%). Adnet et al.[25] showed that difficulty in intubation is usually encountered in poisoning patients with GCS scores between seven and nine. Intubation of such patients is generally facilitated by appropriate sedation and/or neuromuscular blockade. Emerman et al.[26] concluded that a GCS score of less than eight was the most sensitive predictor of serious complications (sensitivity = 86%, specificity = 89%) e.g. in tricyclic antidepressant overdose. Grmec et al.[10] found that good sensitivity and specificity existed for GCS score in predicting respiratory failure and showed it to be relatively good in predicting in-hospital mortality following OP poisoning.

The acute physiology and chronic health evaluation II (APACHE II) system is one of the several ICU scoring systems which can be used to measure the severity of disease and to describe the morbidity and prognosis of patients. The APACHE II scores helps to predict the probability of mortality through the estimate of severity of a disease. Ideal when applied for patients, aged 15 or older, it is used to describe the morbidity of a patient as compared to the outcome of other patients. The predicted mortality rates are averaged for groups of patients in order to specify the group's morbidity. Even though newer scoring systems, including SAPS II, have replaced APACHE II in many places, APACHE II continues to be used extensively because it is the basis of much documentation. The APACHE II system incorporates physiologic variables, age, and a chronic health evaluation into a measure of the risk of mortality; the higher the score the worse the prognosis. In our study the APACHE II scores correlated linearly ($r = 0.347$) with the outcome. Sungurtekin et al.[27] observed a significant correlation between the mortality and scoring scales systems, including APACHE II, GCS, APACHE III and SAPS II and hence recommended the assessment of APACHE II scores in OP poisoning patients. When calculated within 24 h of admission, APACHE II scores significantly differed with the various outcome measures. Our study showed a significant ($P < 0.001$) linear correlation between APACHE II scores and the PSS scores, but there was no association of APACHE II scores with the outcome. The probable reason for failure in predicting the actual outcome may be due to the fact that the intermediate syndrome of OP poisoning usually develops at a later stage, i.e. between the acute cholinergic crisis of fasciculation, muscle weakness and delayed neuropathy. In our study the onset of most symptoms ranged from 8 to 72 h. The APACHE II scores of those patients who died were lower than those observed in other studies, probably due to differences in critical care practices. The scores were however higher among the intubated patients as compared to those who survived without intubation. The significant ($P < 0.001$) correlation between APACHE II scores and the severity, observed in our study were similar to that observed in studies carried out by Eizadi-Mood et al.[28]

The poisoning severity score (PSS) is a severity grading scale adopted by the IPCS, the Commission of the European Union, and the European Association of Poison Centers and Clinical Toxicologists (IPCS/EC/EAPCCT) for grading the severity of poisoning. This scale is necessary to facilitate comparability of case data. The PSS was developed, so that valid comparisons regarding severity and outcome could be made among the various poison centers and to take an account of the overall clinical picture. Therefore the prospective follow-up of cases to establish the most severe symptoms and signs is an integral part of the assessment. The PSS also identifies the more serious cases that are likely to provide more useful clinical data for epidemiological purposes. The purpose of the PSS is to provide a simple but relatively robust system for describing the severity of poisoning on the basis of clinical observations. It is not a prognostic score but is instead meant to define the degree of severity when the overall clinical features are most severe, and will normally require a follow-up of cases.[7] The present study has tried to assess the concordance of severity grading with respect to other specific grading scales including GCS, APACHE, PMR; butyrylcholinesterase indices and outcome. A study by Pach et al. (1999).[29] has reported that the PSS is useful in assessing severity on the basis of observed clinical signs and symptoms (at their maximum), but does not take into account potential risks or plasma/serum concentrations. Other scales suggested for assessing the severity of OP poisoning are the 'Kraków' scale which includes both clinical symptoms on admission and results of toxicological

analyses and the Alert verbal painful unresponsive (AVPU) scale.[21] Studies are also required to assess the reproducibility and predictive value of such evaluation scales with clinical signs and investigations especially among South Asian population. Further prospective studies are required to accurately identify the concordance between PSS and observed mortality in developing countries like India. Such studies could be helpful in the development, implementation and assessment of effectiveness of medical management guidelines.

Some of the identified limitations of the present study included the following. The severity scores including GCS, APACHE II scores and PSS scores were not recorded sequentially during the course of hospitalization or at the time of discharge, as all the biochemical investigations could not be carried out regularly for each and every patient during the hospitalization period. Further, the study results cannot be extrapolated to the whole population, as the sample size was relatively small.

The scoring systems can be effective in the establishment of a clinical database to support effective management of OP pesticide poisoning. Systematically collected data in the form of toxidromes can assist in the clinical evaluation of severity and therefore in implementing evidence-based medical management guidelines. It is likely that these findings reflect a similar situation in many rural hospitals of the Asia Pacific region. Community level preventive measures can be achieved through the study of toxic exposures by setting up surveillance mechanisms and clinical databases on pesticides, by training within the health sector, and by creating awareness through public education and prevention campaigns. The clinical indices including Glasgow coma scale, APACHE II scores, predicted mortality rate and poison severity scores are highly recommended in routine practice to decide the intensity of therapy and can be effectively employed at the time of triage of OP poisoning, especially during terrorism of mass destruction.

6. Conclusions

In the present study the effectiveness of various severity and prognostic scales in evaluating acute OP poisoned patients at the time of admission were evaluated. The clinical characteristics, severity and outcome following hospitalization were assessed. The Class I pesticides considered as extremely hazardous were implicated in a majority of the cases. The clinical indices, GCS, APACHE II score, and PMR significantly ($p < 0.001$) correlated with PSS scores thereby indicating their usefulness to predict severity. The mean hospitalization period and outcome of poisoning were significantly influenced by the PSS scores but not by the APACHE II or GCS scores. The findings of this study highlights the usefulness of few clinical indices like GCS, APACHE II, PMR and Poisoning severity scoring systems for predicting severity which in turn can be used to predict outcome of poisoning in patients especially during triage. Identification of severity at an early stage followed by prompt treatment can prevent the late respiratory and cardiac failures associated with OP poisoning.

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